Laparoscopic Versus Open Appendectomy in Children

A Meta-Analysis

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Objective: This study aims to use meta-analysis to compare laparoscopic and open appendectomy in a pediatric population.

Summary Background Data: Meta-analysis is a statistical tool that can be used to evaluate the literature in both qualitative and quantitative ways, accounting for variations in characteristics that can influence overall estimate of outcomes of interest. Meta-analysis of laparoscopic versus open appendectomy in a pediatric population has not previously been performed.

Methods: Comparative studies published between 1992 and 2004 of laparoscopic versus open appendectomy in children were included. Endpoints were postoperative pyrexia, ileus, wound infection, intra-abdominal abscess formation, operative time, and postoperative hospital stay.

Results: Twenty-three studies including 6477 children (43% laparoscopic, 57% open) were included. Wound infection was significantly reduced with laparoscopic versus open appendectomy (1.5% versus 5%; odds ratio [OR] = 0.45, 95% confidence interval [CI], 0.27–0.75), as was ileus (1.3% versus 2.8%; OR = 0.5, 95% CI, 0.29–0.86). Intra-abdominal abscess formation was more common following laparoscopic surgery, although this was not statistically significant. Subgroup analysis of randomized trials did not reveal significant difference between the 2 techniques in any of the 4 complications. Operative time was not significantly longer in the laparoscopic group, and postoperative stay was significantly shorter (weighted mean difference, −0.48; 95% CI, −0.65 to −0.31). Sensitivity analysis identified lowest heterogeneity when only randomized studies were considered, followed by prospective, recent, and finally large studies.

Conclusions: The results of this meta-analysis suggest that laparoscopic appendectomy in children reduces complications. However, we also see the need for further high-quality randomized trials comparing the 2 techniques, matched not only for age and sex but also for obesity and severity of appendicitis.

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Open appendectomy (OA) as first described in the 19th century[1,2] performed through the right lower quadrant incision has remained mainly unchanged until the introduction of laparoscopic appendectomy (LA) in 1983.[3] Since then, much debate has centered on which technique is the preferable mode of removing the inflamed appendix. Although LA has gained much popularity among some surgeons, others remain skeptical of replacing the relatively straightforward OA. Criticism of the LA includes increased operative cost, primarily due to the use of disposable laparoscopic instruments,[4] increased operative time, and concerns about a higher incidence of intra-abdominal abscesses, particularly after perforated appendicitis.[5] Proponents of LA, however, claim that the advantages of the procedure include improved wound healing, reduced postoperative pain,[4,6] and ultimately earlier discharge from hospital,[7] all translating to an earlier return to normal activity.[8] They also support the idea of laparoscopically evaluating the peritoneal cavity prior to committing to appendectomy, particularly in difficult cases.

In the pediatric population, appendectomy is one of the most common emergency operations, yet in children, the benefits of LA as compared with OA remain undefined. Children represent a group of patients who would benefit greatly from reduced postoperative complications, earlier mobilization, and ultimately discharge from hospital, particularly because of the potential disruptive effect of illness on their lives. Although much research has been done to compare results from LA and OA in children, conclusions have been difficult to draw because of small study size, presence of only a handful of randomized trials, and possible heterogeneity in patient characteristics, surgical practice, and severity of appendicitis between these studies. At present, therefore, there is no consensus between pediatric surgeons as to the benefits of LA over OA.

Meta-analysis is a useful statistical tool that can be used to evaluate the existing literature in both a qualitative and quantitative way by comparing and integrating the results of

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different studies, taking into account variations in characteristics that can influence the overall estimate of the outcome of interest. We have previously used meta-analytic techniques to evaluate successfully the impact of minimally invasive procedures in routine practice.[9,10] In addition, although meta-analysis of randomized prospective research comparing LA to OA in an adult population has suggested clear benefits of the laparoscopic surgery,[6,11–15] none of these studies has commented on outcomes for the pediatric age-group and the factors that cause heterogeneity between studies included in their analyses. Finally, in the last 2 years, a number of high-quality comparative studies of LA versus OA have been published and should be taken into account.

This study aims to use meta-analysis to compare laparoscopic versus open appendectomy in a pediatric population, with regard to postoperative complications, length of hospital stay, and operative time. The specific questions that our study aims to answer are: 1) Does LA significantly reduce the postoperative wound infection rate in comparison to OA? 2) Is the incidence of intra-abdominal abscess following LA significantly different to that following OA? 3) Is there a significant difference in the incidence of early postoperative complications such as ileus and fever with LA as compared with OA? 4) Is there significant heterogeneity in the estimates of the outcomes of interest between studies OA and LA, and how can this be explained? 5) Is the operative time taken for LA significantly greater than OA? 6) Is LA associated with a reduced length of postoperative stay following appendectomy?

MATERIALS AND METHODS

Study Selection

A Literature search was performed using Embase, Medline, Cochrane, and Pubmed databases, on all studies published between 1992 and 2004 reporting on laparoscopic surgery for appendicitis, and comparing this to conventional open appendectomy. The following Mesh search headings were used: "comparative studies and appendectomy," "pediatric/paediatric and laparoscopic and appendicectomy/appendectomy," and "minimally invasive and pediatric/paediatric and appendicectomy/appendectomy." Searches were also performed under the terms "laparoscopic versus open appendicectomy/appendectomy" and "minimally invasive versus conventional appendicectomy/appendectomy." The "related articles" function was used to broaden the search, and all abstracts, studies, and citations scanned were reviewed.

Data Extraction

Two reviewers (O.A. and T.A.) independently extracted the following data from each study: first author, year of publication, study population characteristics, study design, severity of appendicitis, number of subjects operated on with each technique, and conversion rate from LA to OA.

Inclusion Criteria

To enter our analysis, studies had to:

1. Report the operative results on a "pediatric population" or use the word "children" to describe the study group.
2. Compare LA and OA techniques.
3. Report on at least one of the outcome measures mentioned below.
4. Contain a previously unreported patient group (if patient material was reported more than once, we chose the most informative and recent article).
5. When 2 studies were reported by the same institution, our analysis included either the one of better quality, or the most recent publication.

Exclusion Criteria

The following criteria were used to exclude studies from our analysis:

1. Studies in which the outcomes of interest (mentioned below) were not reported for the 2 techniques or it was impossible to calculate these from the published results.
2. Studies that used variations on the standard laparoscopic technique, including hybrid procedures (laparoscope-assisted appendectomy) and single trochar techniques involving delivery of the appendix into the abdominal wound followed by open appendectomy.
3. Studies in which the standard deviation of the mean for continuous outcomes of interest (length of stay and operative time) were not reported.

Outcomes of Interest and Definitions

LA and OA were compared with regards to several postoperative complications ranging from immediate to late, as mentioned in the selected studies including: "postoperative fever," "postoperative ileus," "wound infection," and "intra-abdominal abscess formation." These complications were not further defined in any of the studies. We were also interested in collecting data on the operative time taken and postoperative length of hospital stay following LA versus OA techniques.

Statistical Analysis

Meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Quality of Reporting of Meta-analyses (QUORUM) guidelines.[16,17] Statistical analysis for categorical variables was carried out using the odds ratio as the summary statistic. This ratio represents the odds of an adverse event occurring in the treatment (LA) group compared with the reference (OA) group. An odds ratio of less than one favors the treatment group, and the point estimate of the odds ratio is considered statistically significant at the $P < 0.05$ level if the 95% confidence interval does not include the value one.

The Mantel-Haenszel method was used to combine the odds ratio for the outcomes of interest. Yates' correction was used for those studies that contained a zero in one cell for the number of events of interest in one of the 2 groups.[18,19] These "zero cells" create problems with the computation of ratio measure and its standard error of the treatment effect. This was resolved by adding the value 0.5 in each cell of the 2×2 table for the study in question; and if there were no events for both LA and OA groups, the study was discarded from the meta-analysis.

In this study, both fixed and random effect models were used. In a fixed effect model, it is assumed that the treatment effect in each study is the same; whereas in a random effect model, it is assumed that there is variation between studies and the calculated odds ratio thus has a more conservative value.[20,21] In surgical research, meta-analysis using the random effect model is preferable, particularly because patients that are operated on in different centers have varying risk profiles and selection criteria for each surgical technique.

In the tabulation of our results (Fig. 1), squares indicate point estimates of treatment effect (odds ratio), with 95% confidence intervals indicated by horizontal bars. The diamond represents the summary odds ratio from the pooled studies with 95% confidence intervals. For continuous variables such as length of stay and operative time, statistical analysis was carried out using the random effect weighted mean difference as the summary statistic.[20] In Figures 2 and 3, squares indicate point estimates of treatment effect (weighted mean difference), with the size of the square representing the weight attributed to each study and 95% confidence intervals indicated by horizontal bars. The diamond represents the summary from the pooled studies with 95% confidence intervals. The point estimate is considered statistically significant at the $P < 0.05$ level if the 95% confidence interval does not include the vertical bar.

Analysis was conducted by using the statistical software SPSS version 10.0 for Windows (SPSS Inc., Chicago, IL), Intercooled Stata version 7.0 for Windows (Stata Corporation, USA), Review Manager Version 4.2 (Cochrane Collaboration, Software Update, Oxford) and the Sample Power 2.0 (SPSS Inc., Chicago, IL) for power analysis calculations.

Three strategies were used to quantitatively assess heterogeneity. First, data were reanalyzed using both fixed and random effect models. Second, graphical exploration with funnel plots was used to evaluate publication bias.[20,22] Third, sensitivity analysis was undertaken using subgroup analysis. To do this, the following variables were evaluated: 1) all studies, 2) study size (more than 50 patients in each arm), 3) year of publication (inclusive of or greater than 2000), 4) prospective studies, and 5) randomized studies.

To translate these results into benefits to clinical outcome, the following parameters were calculated: Absolute risk reduction (ARR) which in this case is the difference in the incidence of postoperative complications between LA and OA groups, and number needed to treat (NNT), which is the number of patients who must be treated (using LA) to prevent one complication event (NNT = 1/ARR).

Sample Size Considerations

The overall incidence of postoperative infection between studies in OA was 87 of 1739 (approximately 5%). To rule out a 50% relative risk reduction (from 5% to 2.5%) with a 5% significance level and 80% power, we calculated that a traditional randomized controlled trial would require 984 patients in each arm. For the complications of abscess formation and ileus (whose incidence was lower), the number of patients required in each arm of a randomized trial would be even higher.

RESULTS

Selected Studies

Twenty-seven studies published between 1992 and 2004 matched the inclusion criteria, comparing LA versus OA in a pediatric population, and reporting the incidence of postoperative complications, operative time, or length of postoperative stay.[23–49] Two of these were excluded because they reported their results in a way that data for the outcomes of interest could not be extracted.[33,38] Finally, 3 of the studies were by the same author;[44–46] therefore, we chose the most recent publication.[46] Twenty-three studies therefore matched the selection criteria and were suitable for meta-analysis.[23–32,34–37,39–43,46–49] These included retrospective, prospective nonrandomized and prospective randomized studies, with a combined total of 6477 subjects, of which 2789 (43%) underwent LA and 3688 (57%) OA. On review of the data extraction there was 100% agreement between the 2 reviewers.

The characteristics of these studies are demonstrated in Table 1. The study design was retrospective in 12, prospective in 11, and randomized in 7 studies. Fourteen studies contained at least 50 patients in both LA and OA groups and 14 studies had a recent year of publication (inclusive of or greater than 2000). The age of patients included ranged from 0 to 20 years, and a conversion rate was reported in 14 studies (range, 0%–25.9%). Six studies contained LA and OA groups that were matched for severity of appendicitis. The results from meta-analysis of the studies with regards to individual complications, length of stay, and operative time are summarized below. Figure 1 represents the meta-analytic outcome for the individual complications when all studies were considered, with Figures 2 and 3 representing results from meta-analysis of the continuous variables (length of stay and operative time).

Wound Infection

Thirteen studies reported the incidence of postoperative wound infection,[23,25–28,32,34,36,39,42,46,47,49] with 2 showing a statistically significant reduction in the LA as compared with the OA group.[27,49] Meta-analysis of all studies showed a significantly reduced incidence of wound infection of 1.5% (30 of 2016) in LA compared with 5% (87 of 1739) in OA, odds ratio (OR) of 0.45, and confidence interval (CI) of 0.27 to 0.75. Finally, the absolute risk reduction (ARR) in the LA in comparison to the OA group was calculated to be 0.0351, which can be translated in a number of patients needed to treat (NNT) of 28.

Subgroup analysis of studies with at least 50 patients in each arm[23,25,27,28,32,34,36,47] showed a significantly reduced incidence of wound infection of 1.2% (21 of 1757) with LA as compared with 4.8% (70 of 1472) with OA (OR = 0.46; CI, 0.27–0.80), which was reproduced when only recent studies[23,25,28,36,39,46,47,49] were considered (wound infection = 1.5% in LA versus 4.9% in OA, OR = 0.48; CI, 0.29–0.81). In meta-analysis of randomized studies,[39,42,46,47] the incidence of wound infection was 1.9% (5 of 262) with LA as compared with 4.7% (24 of 512) with OA, but this was not significant (OR = 0.47; CI, 0.16–1.35). This finding was mirrored in the case of prospective studies[34,36,39,42,46,47]

Review: Surgical technique for appendicectomy in paediatric population
Comparison: 01 POSTOPERATIVE COMPLICATIONS
Outcome: 01 POSTOPERATIVE COMPLICATIONS

Study or sub-category	LAPAROSCOPIC n/N	OPEN n/N	Weight %	OR (random) 95% CI	Year
01 INFECTION					
LEJUS	0/32	0/31		Not estimable	1996
GILCHRIST	0/14	1/50	0.62	1.14 [0.04, 29.46]	1992
HAY	0/34	3/48	0.73	0.19 [0.01, 3.77]	1998
LINTULA	0/43	5/44	0.76	0.08 [0.00, 1.54]	2004
BLAKELY	0/65	12/180	0.80	0.10 [0.01, 1.76]	1998
LITTLE	2/44	1/44	1.08	2.05 [0.18, 23.44]	2002
CANTY	3/955	1/173	1.23	0.54 [0.06, 5.24]	2000
HORWITZ	4/27	1/22	1.23	3.65 [0.38, 35.34]	1997
LEE	1/54	4/59	1.28	0.26 [0.03, 2.40]	2003
VARLET	1/200	11/203	1.48	0.09 [0.01, 0.69]	1993
VEGUNTA	3/65	6/28	2.71	0.18 [0.04, 0.77]	2004
OKA	3/141	15/376	3.54	0.52 [0.15, 1.84]	2004
McKINLAY	8/204	8/119	5.00	0.57 [0.21, 1.55]	2002
PAYA	5/138	19/362	5.01	0.68 [0.25, 1.85]	2000
Subtotal (95% CI)	2016	1739	25.48	0.45 [0.27, 0.75]	
Total events: 30 (LAPAROSCOPIC), 87 (OPEN)					
Test for heterogeneity: Chi² = 13.06, df = 12 (P = 0.36), I² = 8.1%					
Test for overall effect: Z = 3.07 (P = 0.002)					
02 ABSCESS					
GILCHRIST	0/14	1/50	0.62	1.14 [0.04, 29.46]	1992
LEE	1/54	0/59	0.63	3.34 [0.13, 83.66]	2003
LINTULA	1/43	0/44	0.63	3.14 [0.12, 79.26]	2004
PAYA	0/138	4/362	0.76	0.29 [0.02, 5.38]	2000
LITTLE	1/44	1/44	0.83	1.00 [0.06, 16.51]	2002
HAY	1/34	2/48	1.07	0.70 [0.06, 8.01]	1998
VEGUNTA	6/65	1/28	1.35	2.75 [0.31, 23.94]	2004
PLATTNER	1/58	8/92	1.42	0.18 [0.02, 1.51]	1997
VARLET	2/200	4/203	2.08	0.50 [0.09, 2.77]	1993
HORWITZ	11/27	2/22	2.23	6.88 [1.33, 35.58]	1997
MEGUERDITCHIAN	2/126	6/262	2.30	0.69 [0.14, 3.46]	2002
KOTLOBOVSKY	4/100	4/100	2.89	1.00 [0.24, 4.11]	2003
McKINLAY	7/204	8/119	4.76	0.49 [0.17, 1.40]	2002
CANTY	24/955	6/173	5.80	0.72 [0.29, 1.78]	2000
OKA	9/141	14/376	6.26	1.76 [0.75, 4.17]	2004
DRONOV	18/100	9/100	6.33	2.22 [0.94, 5.21]	2000
Subtotal (95% CI)	2303	2082	39.95	1.11 [0.73, 1.71]	
Total events: 88 (LAPAROSCOPIC), 70 (OPEN)					
Test for heterogeneity: Chi² = 18.02, df = 15 (P = 0.26), I² = 16.8%					
Test for overall effect: Z = 0.50 (P = 0.62)					
03 OBSTRUCTION/ILEUS					
HAY	0/34	1/48	0.63	0.46 [0.02, 11.61]	1998
OKA	0/141	1/376	0.64	0.88 [0.04, 21.84]	2004
MEGUERDITCHIAN	0/126	2/262	0.71	0.41 [0.02, 8.64]	2002
VARLET	0/200	4/203	0.76	0.11 [0.01, 2.07]	1993
CANTY	8/955	1/173	1.44	1.45 [0.18, 11.69]	2000
PAYA	1/138	12/362	1.49	0.21 [0.03, 1.65]	2000
PLATTNER	2/58	3/92	1.85	1.06 [0.17, 6.54]	1997
McKINLAY	7/204	8/119	4.76	0.49 [0.17, 1.40]	2002
DRONOV	8/100	16/100	5.90	0.46 [0.19, 1.12]	2000
Subtotal (95% CI)	1956	1735	18.17	0.50 [0.29, 0.86]	
Total events: 26 (LAPAROSCOPIC), 48 (OPEN)					
Test for heterogeneity: Chi² = 3.58, df = 8 (P = 0.89), I² = 0%					
Test for overall effect: Z = 2.49 (P = 0.01)					
04 FEVER					
GILCHRIST	1/14	7/50	1.32	0.47 [0.05, 4.20]	1992
LITTLE	21/44	25/44	6.47	0.69 [0.30, 1.61]	2002
PAYA	12/138	46/362	8.61	0.65 [0.34, 1.28]	2000
Subtotal (95% CI)	196	456	16.40	0.66 [0.40, 1.09]	
Total events: 34 (LAPAROSCOPIC), 78 (OPEN)					
Test for heterogeneity: Chi² = 0.10, df = 2 (P = 0.95), I² = 0%					
Test for overall effect: Z = 1.62 (P = 0.11)					

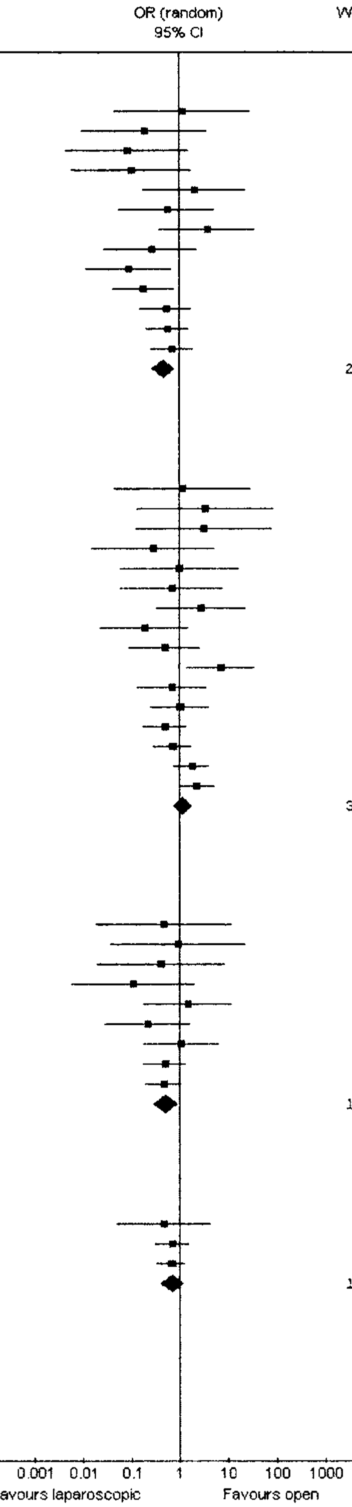
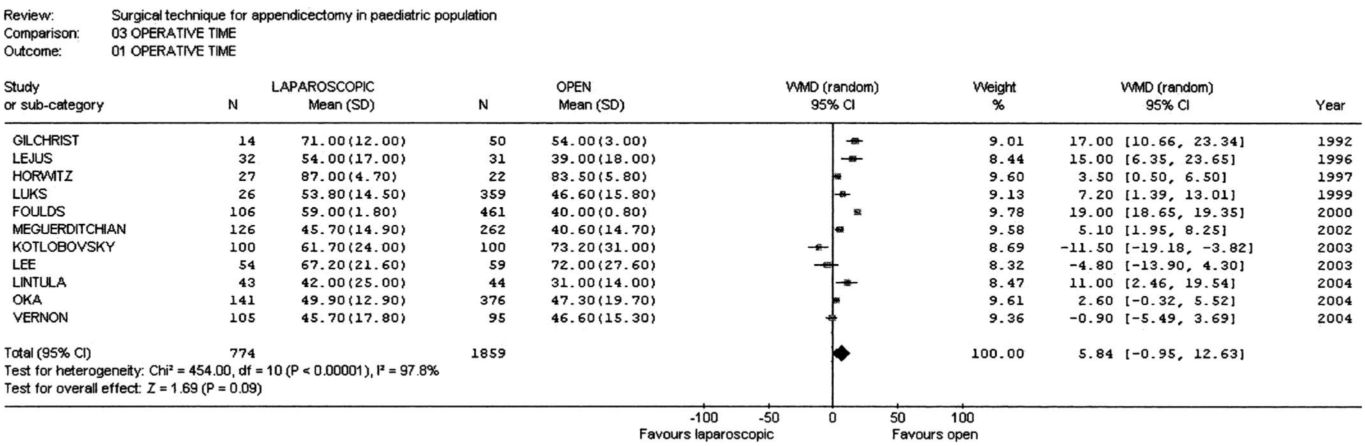
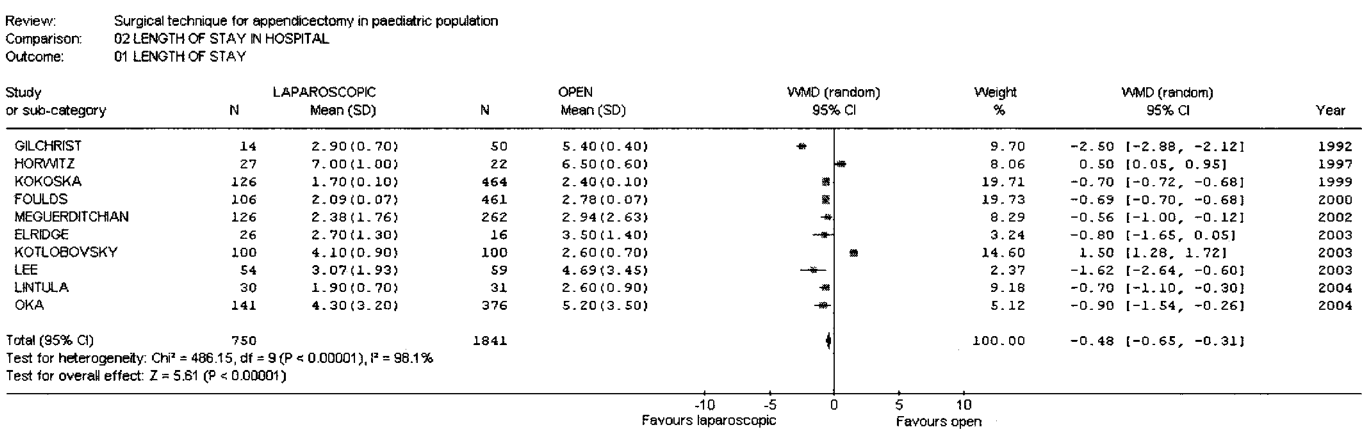


FIGURE 1. Meta-analysis of all studies comparing postoperative complications between LA and OA techniques.



Study or sub-category	Laparoscopic N	Laparoscopic Mean (SD)	Open N	Open Mean (SD)	Weight %	WMD (random) 95% CI	Year
GILCHRIST	14	71.00(12.00)	50	54.00(3.00)	9.01	17.00 [10.66, 23.34]	1992
LEJUS	32	54.00(17.00)	31	39.00(18.00)	8.44	15.00 [6.35, 23.65]	1996
HORWITZ	27	87.00(4.70)	22	83.50(5.80)	9.60	3.50 [0.50, 6.50]	1997
LUKS	26	53.80(14.50)	359	46.60(15.80)	9.13	7.20 [1.39, 13.01]	1999
FOULDS	106	59.00(1.80)	461	40.00(0.80)	9.78	19.00 [18.65, 19.35]	2000
MEGUERDITCHIAN	126	45.70(14.90)	262	40.60(14.70)	9.58	5.10 [1.95, 8.25]	2002
KOTLOBOVSKY	100	61.70(24.00)	100	73.20(31.00)	8.69	-11.50 [-19.18, -3.82]	2003
LEE	54	67.20(21.60)	59	72.00(27.60)	8.32	-4.80 [-13.90, 4.30]	2003
LINTULA	43	42.00(25.00)	44	31.00(14.00)	8.47	11.00 [2.46, 19.54]	2004
OKA	141	49.90(12.90)	376	47.30(19.70)	9.61	2.60 [-0.32, 5.52]	2004
VERNON	105	45.70(17.80)	95	46.60(15.30)	9.36	-0.90 [-5.49, 3.69]	2004
Total (95% CI)	774		1859		100.00	5.84 [-0.95, 12.63]	

FIGURE 2. Meta-analysis of studies comparing operative time between LA and OA techniques.



Study or sub-category	Laparoscopic N	Laparoscopic Mean (SD)	Open N	Open Mean (SD)	Weight %	WMD (random) 95% CI	Year
GILCHRIST	14	2.90(0.70)	50	5.40(0.40)	9.70	-2.50 [-2.88, -2.12]	1992
HORWITZ	27	7.00(1.00)	22	6.50(0.60)	8.06	0.50 [0.05, 0.95]	1997
KOKOSKA	126	1.70(0.10)	464	2.40(0.10)	19.71	-0.70 [-0.72, -0.68]	1999
FOULDS	106	2.09(0.07)	461	2.78(0.07)	19.73	-0.69 [-0.70, -0.68]	2000
MEGUERDITCHIAN	126	2.38(1.76)	262	2.94(2.63)	8.29	-0.56 [-1.00, -0.12]	2002
ELRIDGE	26	2.70(1.30)	16	3.50(1.40)	3.24	-0.80 [-1.65, 0.05]	2003
KOTLOBOVSKY	100	4.10(0.90)	100	2.60(0.70)	14.60	1.50 [1.28, 1.72]	2003
LEE	54	3.07(1.93)	59	4.69(3.45)	2.37	-1.62 [-2.64, -0.60]	2003
LINTULA	30	1.90(0.70)	31	2.60(0.90)	9.18	-0.70 [-1.10, -0.30]	2004
OKA	141	4.30(3.20)	376	5.20(3.50)	5.12	-0.90 [-1.54, -0.26]	2004
Total (95% CI)	750		1841		100.00	-0.48 [-0.65, -0.31]	

FIGURE 3. Meta-analysis of studies comparing length of stay between LA and OA techniques.

where the incidence of wound infection was 2.4% (10 of 414) in LA versus 4.8% (44 of 924) in OA (OR = 0.58; CI, 0.29–1.16).

Intra-abdominal Abscess

Sixteen studies reported the incidence of intra-abdominal abscess formation,[23,25–28,30,34–36,39–42,46,47,49] with only one individually showing a significant difference between LA and OA groups.[26] Meta-analysis of all studies (incidence of 3.8%; 88 of 2303) in LA versus 3.4% (70 of 2082) in OA (OR = 1.11; CI, 0.73–1.71) and of only prospective studies[34–36,39–42,46,47] (incidence of 3.6%; 27 of 740) in LA versus 2% (28 of 1386) in OA (OR = 1.34; CI, 0.75–2.39) did not reveal any significant difference between groups. Considering only randomized studies[39–42,46,47] gave an incidence of 7.4% (34 of 462) with LA compared with 4.2% (30 of 712) with OA (OR = 1.70; CI, 1–2.87). Similar results were achieved following subgroup analysis of studies containing a group of at least 50 patients in each arm[23,25,27,28,30,35,36,40,41,47] (incidence of 1.3% in LA versus 3.4% in OA; OR = 0.94; CI, 0.58–1.51), and when only recent studies[23,25,28,35,36,39–41,46,47,49] were considered (incidence of 3.7% in LA versus 3.2% in OA; OR = 1.16; CI, 0.78–1.73).

Postoperative Ileus

Nine studies reported the incidence of postoperative ileus,[23,25,27,30,35,36,41,42,47] with none individually showing a statistically significant reduction in the LA versus OA. Meta-analysis of all studies showed a significantly reduced incidence of 1.3% (26 of 1956) in LA versus 2.8% (48 of 1735) in OA (OR = 0.5; CI, 0.29–0.86), as did analysis of the prospective studies,[23,35,36,41,42,47] where incidence of postoperative ileus was 2.2% (16 of 743) in LA versus 3.2% (40 of 1267) in OA (OR = 0.45; CI, 0.24–0.82). In the case of postoperative ileus, the ARR in the LA in comparison to the OA group was calculated to be 0.0145, which can be translated into a NNT of 69.

Meta-analysis of the 3 randomized studies[41,42,47] showed an incidence of 2.9% (8 of 275) with LA and 3.4% (18 of 524) with OA (OR = 0.48; CI, 0.21–1.10), which was not statistically significant. Considering only studies with a group of at least 50 patients in each arm[23,25,27,30,35,36,41,47] calculated a significantly lower incidence of 1.4% (26 of 1922) in LA versus 2.8% (47 of 1687) in OA (OR = 0.5; CI, 0.29–0.87). Meta-analysis of the 6 recent studies[23,25,35,36,41,47] showed a significantly favorable outcome toward LA with an incidence of 1.4% (24 of 1664) as

TABLE 1. Study Characteristics

Reference (Year)	Study Type	Cases OA	Cases LA	Age (Year)	Mean Cost of Hospital Stay ($)	Matching†	Conversion Rate (%)	Severity (% Gangrene, Perforation, Abscess) OA	Severity (% Gangrene, Perforation, Abscess) LA
Gilchrist (1992)	PNR	50	14	OA 9.7/LA 9.8	OA $5515/LA $5935	1,2,3,4,5,6	—	32	36
Lejus (1996)	PR	31	32	8–15	—	5,6,7	0	12.90	12.50
Varlet* (1993)	R	203	200	1.75–16	—	5,7	5		—
Horwitz* (1997)	R	22	27	2–16	—	None	25.9	100	100
Luks (1999)	R	359	26	0–17	—	5,6,7	—	—	—
Kokoska (1999)	R	464	126	<15	—	7	—	—	—
Foulds (2000)	R	461	106	<16	—	None	19.1	17.35	8.49
Blakely (1998)	R	180	65	9.8	—	None	—		—
Plattner* (1997)	R	92	58	1–15	—	5,7	12	100	100
Hay (1998)	PR	48	34	4–12	—	1,2,3	0	—	—
Canty (2000)	R	173	955	1.17–19	—	None	1.1	50.29	31.62
Dronov (2000)	PR	100	100	—	—	None	—	—	—
Paya (2000)	PNR	362	138	0–19	—	None	4.4	—	—
Little* (2002)	PR	44	44	1–16	OA $7091/LA $8041	None	6.8	25	22.73
Meguerditchian (2002)*	PNR	262	126	0–16	—	None	2.4	7.63	14.29
								14.89	10.32
Eldridge (2003)	PNR	16	26	8–15	—	4,6,7	—		0
McKinlay* (2003)	R	119	204	1–18	—	1,7	0.3	59	23
Kotlobovsky (2003)	PR	100	100	0–16	—	None	2.1	—	—
Lee (2003)	R	59	54	<18	—	5,6	5.6	—	—
Lintula* (2004)	PR	44	43	4–15	—	5,6,7	—	75	81.40
Oka* (2004)	PR	376	141	2–20	—	3,5,7	—	30.3	30.5
Vernon* (2004)	R	95	105	0–16	OA $4472/LA $5510	5,7	—	—	—
Vegunta* (2004)	R	28	65	10 (median)	OA $1858/LA $3718	5,7	4.6	—	—

*Study that stated use of postoperative antibiotics in all cases of appendicitis.
†Matching: 1, fever; 2, WCC; 3, peritonitis; 4, duration; 5, age; 6, weight; 7, sex.
R indicates retrospective; PNR, prospective nonrandomized; PR, prospective randomized; S, severe cases only; LOS, length of stay; OA, open appendectomy; LA, laparoscopic appendectomy.

compared with 2.9% (40 of 1392) with OA (OR = 0.49; CI, 0.27–0.89).

Postoperative Fever

Only 3 studies reported the incidence of postoperative fever,[34,36,39] all of which were of prospective design, with none individually showing a significant difference with LA versus OA. Meta-analysis of these studies did not show a significant difference in incidence postoperative fever between the 2 groups (17.3%; 34 of 196) in LA versus 17.1% (78 of 456) in OA (OR = 0.66; CI, 0.40–1.09). Only one study was randomized[39] and one contained sample groups of greater than 50 patients;[36] therefore, meta-analysis of these subgroups was not possible. Two studies had a year of publication equal to or greater than 2000, with meta-analysis showing an incidence of postoperative fever 33 of 182 (18.1%) in LA and 71 of 406 (17.5%) in OA (OR = 0.67; CI, 0.40–1.13).

Meta-Analysis of Randomized Trials

When only randomized studies were considered, there was also no significant difference between groups with regards to the 4 complications of interest. The incidence of infection was 1.9% (5 of 262) with LA versus 4.7% (24 of 512) in OA (OR = 0.47; CI, 0.16–1.35), abscess was 7.4% (34 of 462) with LA versus 4.2% (30 of 712) in OA (OR = 1.7; CI, 1–2.87), and postoperative ileus was 2.9% (8 of 275) with LA versus 3.4% (18 of 524) in OA (OR = 0.48; CI, 0.21–1.1). Only one randomized study reported postoperative pyrexia.[39]

Operative Time

Eleven of 23 studies included in the meta-analysis reported operative time in LA versus OA groups.[26,28,29,31,34,35,40,43,46,47,48] The results (Fig. 2) did not show a significantly greater length of operation in the laparoscopic versus the open group, random-effect weighted mean difference of 5.84 (CI, −0.95 to 12.63).

Length of Hospital Stay

Ten studies reported postoperative length of stay in LA versus OA groups.[24,26,28,29,31,34,35,40,46,47] The results (Fig. 3) showed a significant reduced postoperative hospital stay in the laparoscopic versus open appendectomy, with random-effect weighted mean difference of −0.48 (CI, −0.65 to −0.31).

Sensitivity Analysis

The results for sensitivity analysis using fixed and random effect models for each of the 4 complications are shown in Table 2. We have previously discussed the preference of using random over fixed effects models in surgical statistical analyses and will therefore mention only the former in the results below.

With regards to wound infection, the sensitivity analysis results showed that the lowest heterogeneity (HG) was identified when only randomized trials were considered (HG = 3.22, $P = 0.36$), findings that were also noted when only prospective studies were considered (HG = 3.64, $P = 0.60$). Considering studies of more than 50 patients in each arm resulted in a large number of patients in LA (1757) and OA (1472) groups, while still maintaining relatively low heterogeneity (HG = 4.92, $P = 0.55$). In the case of intra-abdominal abscess formation, the lowest HG was also identified when only randomized trials were considered (HG = 1.71, $P = 0.89$). Not unexpectedly, this was also low with prospective studies (HG = 3.89, $P = 0.87$) and only next lowest when only studies with year of publication equal to or greater than 2000 considered (HG = 9.51, $P = 0.48$). This finding was repeated in the case of postoperative ileus with lowest HG found in randomized studies (HG = 0.15, $P = 0.93$), followed by prospective (HG = 0.73, $P = 0.98$) and then recently published studies (HG = 1.86, $P = 0.87$). Finally, with regards to postoperative fever, heterogeneity was low because of the small number of studies reporting this complication (prospective studies: HG = 0.10, $P = 0.95$). The above findings highlight the paramount importance of accounting for good study design, adequate sample size, and finally the effects of time when comparing new surgical techniques.

A "funnel plot" of the 23 studies used in our meta-analysis are shown in Figure 4a. This is scatter plot of the treatment effects estimated from individual studies on the horizontal axis (OR), against a measure of study size on the vertical axis (SE[logOR]). The plot resembles a symmetric inverted funnel (the 95% confidence interval). The name "funnel plot" is based on the fact that precision in the estimation of the underlying treatment effect will increase as the sample size of the component studies increases. Figure 4b represents a similar funnel plot, but this time including only randomized studies. It is notable that in the second funnel plot, only one study lies outside the 95% CI axis in comparison to Figure 4a where 3 studies are outside the 95% CI axis.

Cost of Hospital Stay

Only 4 of the studies gave mean costs for hospital stay in LA versus OA groups, all of which were performed in the United States. Although the instruments used were slightly different in these studies, the mean cost of OA for these studies was \$4734 (±\$2199) versus a mean cost for LA of \$5801 (±\$1776). Interestingly however, the reported hospital cost for LA in 1992 has been reported as \$5935,[34] whereas a recent study published in 2004 reported their LA hospital cost as being \$3718,[49] a difference of \$2217.

DISCUSSION

The results of this meta-analysis of 23 studies (retrospective, prospective, and randomized) suggest that the postoperative complications of wound infection and ileus are reduced in children undergoing LA as compared with OA. The incidence of intra-abdominal abscess when all studies were considered was similar (3.8% LA, 3.4% OA); but when only randomized studies were considered this increased in the laparoscopic group (7.4% LA, 4.2% OA), although none of these differences were statistically significant. The incidence of postoperative fever was also not significantly different with laparoscopic versus open surgery, although it must be noted that the number of studies reporting this complication were small. The use of meta-analytic techniques allowed inclusion of a total of 6477 subjects, of which 2789 (43%) underwent LA and 3688 (57%) underwent OA. A sample group this size would otherwise be impossible to accumulate in a reasonable length of time in a randomized control trial. Finally, also noteworthy is the fact that subgroup analysis of only randomized trials did not reveal any significant difference between LA and OA in any of the 4 complication endpoints. These findings should, however, be treated with caution because of the small number of randomized comparative trials of LA versus OA in a pediatric population available for use in the meta-analysis. The results that were calculated for NNT suggest that certain postoperative complications are more likely to be reduced by LA than others. A NNT value of 28 for postoperative wound infection suggests that 28 patients would require the intervention (LA) before benefit was seen. In contrast, for postoperative ileus, the NNT value was much higher at 69.

The answer to the question as to why wound infection might be reduced during LA is unclear. A possible reason for this is that in open appendectomies the appendix is delivered directly through the wound, thereby risking contamination, whereas in laparoscopic surgery this is delivered wither via a bag or into a laparoscopic port. It may also be related to the small size of individual port-site wounds during LA as compared with the longer single wound in OA. Ileus, on the other hand, may be reduced by laparoscopic surgery either because of reduced handling of small and large bowel during the procedure, reduced opiate analgesic requirement in the postoperative period, or because of earlier mobilization. With regards to the case for avoiding LA in perforated or gangrenous appendicitis due to a higher risk of intra-abdominal abscess, our results did not show a statistically significant increase in the rate of intra-abdominal abscess formation in the LA group. We acknowledge that this analysis was unable to match for the severity of appendicitis and that, particularly in the retrospective reports of LA versus OA, the more severe cases of appendicitis may automatically have undergone open surgery, thereby increasing heterogeneity between groups. The finding that incidence of intra-abdominal abscess with the LA was higher than the OA group when only randomized studies were considered should be treated with caution, even though this was not statistically significant (OR = 1.7; CI, 1.0–2.87). Intra-abdominal abscess is a serious complication following appendectomy and, when it occurs, it accounts for

TABLE 2. Results of Sensitivity Analysis for Postoperative Complications

	Wound Infection		Intra-Abdominal Abscess		Ileus		Fever	
	F	R	F	R	F	R	F	R
Overall								
OR	0.41 (0.26–0.64)	0.45 (0.27–0.75)	1.14 (0.81–1.60)	1.11 (0.73–1.71)	0.47 (0.28–0.79)	0.50 (0.29–0.86)	0.65 (0.39–1.09)	0.66 (0.40–1.09)
HG	13.06		18.02		3.58		0.10	
P	0.36		0.26		0.89		0.95	
EV	LA = 30/1984		LA = 88/2303		LA = 26/1956		OA = 34/196	
	OA = 87/1708		OA = 70/2082		OA = 48/1735		LA = 78/456	
Prospective								
OR	0.53 (0.27–1.02)	0.58 (0.29–1.16)	1.30 (0.75–2.25)	1.34 (0.75–2.39)	0.43 (0.23–0.78)	0.45 (0.24–0.82)	0.65 (0.39–1.09)	0.66 (0.40–1.09)
HG	3.64		3.89		0.73		0.10	
P	0.60		0.87		0.98		0.95	
EV	LA = 10/414		LA = 27/740		LA = 16/743		LA = 34/196	
	OA = 44/924		OA = 28/1386		OA = 40/1267		OA = 78/456	
Randomized								
OR	0.41 (0.17–1.03)	0.47 (0.16–1.35)	1.7 (1.01–2.86)	1.7 (1.0–2.87)	0.48 (0.21–1.10)	0.48 (0.21–1.10)	NA	NA
HG	3.22		1.71		0.15		NA	
P	0.36		0.89		0.93		NA	
EV	LA = 5/262		LA = 34/462		LA = 8/275		NA	
	OA = 24/512		OA = 30/712		OA = 18/524			
Size								
OR	0.4 (0.23–0.67)	0.46 (0.27–0.80)	0.96 (0.66–1.4)	0.94 (0.58–1.51)	0.47 (0.28–0.8)	0.50 (0.29–0.87)	NA	NA
HG	4.92		11.88		3.58		NA	
P	0.55		0.22		0.83		NA	
EV	LA = 21/1757		LA = 68/2076		LA = 26/1922		NA	
	OA = 70/1472		OA = 63/1846		OA = 47/1687			
Year of publication								
OR	0.47 (0.28–0.78)	0.48 (0.29–0.81)	1.17 (0.79–1.72)	1.16 (0.78–1.73)	0.48 (0.27–0.84)	0.49 (0.27–0.89)	0.67 (0.40–1.13)	0.67 (0.40–1.13)
HG	5.41		9.51		1.86		0.01	
P	0.61		0.48		0.87		0.91	
EV	LA = 25/1644		LA = 73/1970		LA = 24/1664		LA = 33/182	
	OA = 59/1205		OA = 53/1667		OA = 40/1392		OA = 71/406	

F indocates fixed effect model; R, random effect model; OR, odds ratio (95% CI); HG, heterogeneity (χ^2); *P*, *P* value of heterogeneity; EV, number of adverse events (a patient may have had more than one event); LA, laparoscopic appendicectomy; OA, open appendicectomy; NA, not applicable.

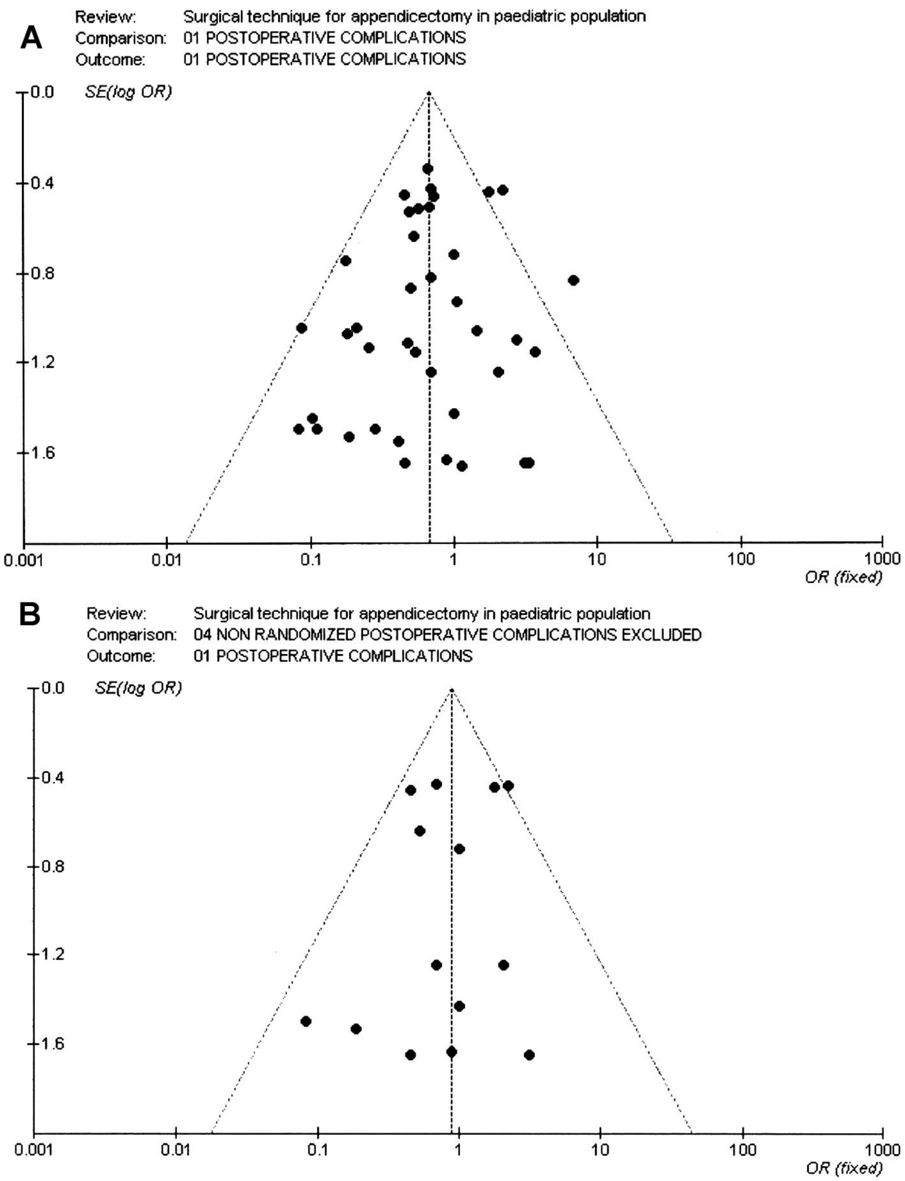


FIGURE 4. A, A "funnel" scatter plot of the all the studies included in our meta-analysis. B, A "funnel" scatter plot including only randomized studies.

significant patient morbidity. Finally, it is important to acknowledge that meta-analysis of randomized studies, where selection bias was not present, did not show any significant difference between LA and OA in the other postoperative complications.

Results for meta-analysis of operative time showed that, although LA took longer than OA, this was not statistically significant. The concept of a laparoscopic procedure taking longer than its open equivalent is not surprising, however, considering the increased instrumentation used during laparoscopic surgery and the setup time involved. Ultimately, the benefit of laparoscopic surgery is unlikely to be the length of the operation, but the quicker healing of smaller operative wounds and earlier recovery. Length of hospital stay results from the studies included in this meta-analysis showed that LA significantly reduced length of hospital stay as compared with OA (Fig. 3) by 0.48 days. These results may be due to the fact that mobilization following LA is improved, thereby facilitating recovery and subsequent discharge from hospital. Why this occurs may be related to wound pain, infection, and ileus formation, all of which impair a patient's mobility following an operation. Although this is a small reduction for a single case, reducing length of stay by this amount for every patient undergoing appendectomy is likely to make a significant difference to cost of postoperative care. Needless to say, this is a link that must be further researched in the future. For children undergoing surgery, the time taken to return to normal activities such as school is of paramount importance, reducing the long-term psychologic effects of hospitalization. Recently, the prospect of performing LA as a "fast-track" operation with postoperative stay <24 hours has been investigated with encouraging results.[50] A final advantage of LA is the ability to perform a diagnostic laparoscopy prior to performing the procedure, which is particularly useful in cases where the diagnosis is less clear.[42] An important hurdle to overcome in performing laparoscopic procedures in the emergency setting, however, is the difficulty in obtaining laparoscopic instruments and trained personnel during nocturnal or holiday periods.

As previously mentioned, meta-analysis has been used in the past to assess LA versus OA in an adult population. This study has investigated the possible benefits of LA in a pediatric population, in whom reduced postoperative complications, earlier mobilization, and shorter hospital stay are particularly desirable. Subgroup sensitivity analysis has also been undertaken to identify sources of heterogeneity for future research on the topic to address. It is important, however, to address the limitations of the meta-analysis, which were as follows: First, different studies may have had slightly different defining criteria for the outcome measures we were interested in. This would particularly apply to postoperative pyrexia, and ileus, as wound infection and intra-abdominal abscess definitions were relatively homogenously reported throughout the studies. In meta-analysis, every attempt is made to select outcome measures that are as absolute as possible, reducing heterogeneity. Second, neither the allocation of treatment nor the assessment of outcome was blinded. Third, it is important to bear in mind nonpublication bias, particularly in meta-analytic research based on published studies. Fourth, there was variation in inclusion criteria, study type, type of randomization, treatment protocols, and outcome assessment between studies. Finally, although the studies included in this meta-analysis reported results on a pediatric population, there were 2 studies that included patients who were clearly over 18 years of age.[25,47] Our reasons for including both studies in the meta-analysis was that they contained patient groups described as "children" who represented a population that was in the pediatric age range with the exception of a few cases, and were undertaken in pediatric centers (San Diego Children's Hospital and Hasbro Children's Hospital, respectively).

Leaving these limitations aside, we think that an important link has been identified between LA and improved wound healing and recovery, when compared with conventional open surgery in a pediatric population. A reduction in postoperative wound infection and ileus has the potential to reduce postoperative pain, allow earlier commencement of oral intake, mobilization, and ultimately results in a reduced length of hospital stay. This also has implications for the total cost of the operation, and although the mean hospital cost of LA ($5801 ± $1776) was greater than OA ($4734 ± $2199), this does not account for the cost of treating postoperative complications such as antibiotics for wound infection, and readmission to hospital. The increased cost of laparoscopic appendectomy is obviously due to the equipment used, with many authors suggesting that using nondisposable laparoscopic instruments may significantly reduce the cost of LA.[31] Although our calculations do not account for inflation, our observation that a hospital cost for LA was $2217 more expensive in a study in 1999 as compared with 2004 suggests that this reduction may already have happened.

In addition to helping to answer the question of whether LA reduces infective and noninfective complications of the procedure, this study raises several important issues regarding the factors that need to be taken into account when comparing the 2 surgical techniques. This is evident in the sensitivity analysis, which shows the level of heterogeneity to be lowest with studies that are of randomized design, followed by prospective studies. We have also highlighted the fact that to further reduce heterogeneity, studies must be of adequate size, and demonstrated that using older publications may increase heterogeneity because surgical technique, degree of proficiency, and types of instrumentation can all change significantly over a period of 5 years. Finally, it is important to note the factors that should be matched for when comparing LA and OA groups. As seen in Table 1, although several studies were matched for age and sex, fewer were matched for severity of appendicitis (represented by fever, raised white cell count, and peritonitis) and weight. We acknowledge that this meta-analysis was unable to account for the effect of severity of appendicitis on the outcome from LA versus OA, which may have altered our conclusions. Both factors (weight and severity) are therefore important when considering postoperative complications, recovery from surgery, and operative time, and must be addressed in future research comparing laparoscopic to open surgery for appendicitis. An additional factor that must be accounted for in future research is the experience of the operating surgeon. Laparoscopic procedures are more likely to be performed by a senior surgeon than open ones, which are often undertaken by the more junior members of the team, a variable that must be accounted for in future comparative research. Finally, results such as those produced by our study may lead to a more accurate informed parental consent when explaining the risks of LA.

Although this study adds weight to the argument that laparoscopic appendectomy in well-selected patients may result in fewer postoperative complications and earlier discharge from hospital, it is important to appreciate that it does not attempt to evaluate the different laparoscopic surgical techniques, port placements, and methods for ligation of the appendix base and meso-appendix. The analysis further highlights the need for high-quality randomized trials, comparing LA to OA in pediatric patient group matched not only for age and sex, but also for obesity and severity of appendicitis.

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